INTERNAL SECRETIONS.

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All tissues of the body produce certain chemical changes as a result of their protoplasmic activity, but in certain cells or aggregations of cells, chemical elaborations have come to be their chief function, the cells having become differentiated in that direction, and the term secreting tissue or gland tissue is applied. The end result of the metabolism in gland tissue is the giving off, or extrusion on the free borders of the cells the products of their activity. These products are known as secretions, and the process itself the act of secretion. Certain secretions are in the nature of waste products of the body, and are not further necessary in the economy of the structure, but are discharged from the body by some avenue, and are known as excretions.

Most secretions accomplish some important and definite office in the economy of the body. Those that are discharged on some free surface, skin or mucous membrane, as sweat, tears, saliva, etc., are called external secretions or true secretions, or commonly called simply secretions.

But our purpose in this article is not to deal with external secretions, but with another class of substances, which we feel sure are elaborated by many of the glandular organs of the body, which conclusion is arrived at from a study of their various manifestations and phenomena.

They are indispensable in the economy of the body, yet little is known of their chemical composition or function. This class of substances we call internal secretions. This term is applicable to all substances which are produced as a result of tissue metabolism, and which, after being poured into the blood, influence in varying degrees the ways of physiologic processes. The idea that secretory products may be given off directly into the blood and lymph has long been held with reference to the ductless glands. The presence of a gland with the absence of a duct for the escape of an external secretion naturally suggested it.

The term, internal secretion, appears to have been first used by Claude Bernard, who emphasized the distinction between ordinary secretion, or external secretion, and the group of internal secretions. However, it is now demonstrated conclusively that some of the glandular organs giving off external secretions, have also an internal secretion. It is maintained by some physiologists that the testes, ovaries, kidney, duodenum, and other glandular organs of the body, not formerly credited with an internal secretion, elaborate substances which produce a characteristic result upon general metabolism.

In some of the ductless glands the existence or absence of an internal secretion is still an open question. Modern interest in internal secretions is largely due to the work of Brown-Sequard, who, as early as 1856, showed by experiments that the removal of the suprarenal glands was followed by the death of the animal. In 1889 he experimented with testicular extracts. This author was led to amplify the conception of an internal secretion by the assumption that all tissues give off something to the blood which is characteristic, and which is of importance in general nutrition. Brown-Sequard was very optomistic with reference to opotherapy, that is, the treatment of diseases of different organs by extracts of the corresponding tissue, but his idea has not yet been fully realized.

Let us consider in detail the character and significance (in so far as we are able), of some of the internal secretions. The glands of the body commonly said to have internal secretions are the thyroid, thymus, adrenals, pituitary body, and to these we add the pancreas, kidneys, ovaries, testes and duodenum. The spleen and liver we might have added to the first group. We shall discuss the secretions of these glands without giving their structure or location, as this would be impracticable in a paper of this kind.

Secretion of the Thyroid.—The most important and definite outcome of the work on internal secretion has been obtained with the thyroid. Exact knowledge of the physiologic purpose of the thyroid dates properly from 1882, when J. L. Reverden drew attention to the profound disturbances which followed the total extirpation of the gland for goitre. However, Schiff, as early as 1856, showed that extirpation of the thyroid in dogs was followed by the death of the animal in from one to four weeks, yet his work was paid little notice at the time. The experiments of Kocher, Gull, Ord and others verified the results obtained by Schiff and Reverden.

All of us are more or less familiar with the train of symptoms first named by Ord, Myxœdema. The condition resulting from a congenital absence of the thyroid gland, or from disease of the gland itself, is relieved by grafting thyroid tissue somewhere in the body of the affected individual, or by feeding him on the glands or extracts of the glands. Many wonderful cures have been effected in this way in the past few years. The treatment, however, must be kept up during life.

How are these phenomena explained? There must be some substance of vital importance in the economy of the body, elaborated by the gland and poured directly into the blood and lymph, an internal secretion. We might well mention here that recently accessory thyroids or parathyroids have been found which are in themselves of great importance. It is now demonstrated that the results following the extirpation of the two differ, but in a study of the secretion we are disregarding the difference in the function between the two glands. It is quite evident that this secretion exercises an important control over the processes of nutrition of the body. There are two general theories advocated as to the manner by which this control is exercised, which theories may also be applied to other internal secretions.

One theory is that the gland elaborates a specific substance containing iodine, and that this secretion is given off to the blood and lymph and carried to the tissues where it exercises an important regulating function upon metabolism. Excision or atrophy of the glands results in the loss of the secretion and a consequent malnutrition or perverted metabolism. Howell thinks this view preferable with the thyroids.

Another theory is that these bodies neutralize or destroy toxic substances formed in the metabolism of the rest of the body. On this theory the removal of the glands results in the accumulation of toxic substances in the body and the animal dies of auto-intoxication.

Adrenals.—Again, it was Brown-Sequard (1856) who first showed that the removal of these bodies was rapidly followed by death often in two or three days, or even in a few hours. It was observed by Addison that a profound disturbance of nutrition, characterized by a bronzing of the skin and mucous membranes, muscular weakness and profound anemia, was associated with pathological conditions of the suprarenal glands. Oliver, Schaffer, and others have verified these experiments. The conclusion is inevitable that the adrenals give off to the blood one or more specifically active substances. An alkaloidal substance was first isolated Abel from extracts of the gland, which was called epinephrin. A crystalizable substance was isolated first by Takamine and later by Aldrich, called adrenalin. The injection of the extracts into the body produces a rapid transitory effect, and up to this time treatment by means of the adrenal extracts has been unsatisfactory. When an injection of the extract is given the animal from which the adrenals have been removed it produces a rise during the usual pre-mortal fall of temperature, and improves the general condition of the animal. The animals become more active, the weakness and uncertainty of movements are diminished and they show a great deal more vigor than before injection.

However, after repeated injections, the effect fails and it is impossible to prolong the life of the animal for more than twenty-four hours (Hultgren, O. Andersen).

When blood from an animal, from which the adrenals have been removed, is injected into an animal operated upon in the same way, the symptoms are increased and its death hastened. This experiment points rather to the theory that this secretion destroys toxic substances in the body.

Thymus Gland and Spleen.—Very little is definitely demonstrated with reference to the function of the thymus gland and spleen. Both are usually spoken of as having internal secretions, yet their character and action remain unsettled.

Pituitary Body.—A number of observers have succeeded in removing the whole of this body, which was followed by a train of symptoms similar to those following thyroidectomy. Recently experiments have been made of injecting extracts of the hypophysis cerebri into the circulation, which was followed by a distinct action upon the heart and blood vessels. According to Vincent and Schaffer we have to do here with two different substances distinguished chemically by their solubility in ether and alcohol, one being soluble and the other not. The first produces a marked fall in blood pressure, while the other increases the pressure and slows and strengthens the heart and produces marked diuresis. This effect is fairly permanent, yet diminishes with repeated injections.

Curiously enough, Howell and others think these substances do not come from the gland proper, but from the posterior or infundibular portion. Acromegally has been associated with disease of this body, but I am able to find no record of improvement by means of injecting extracts from the gland in these cases. cases.

Pancreas.—The internal secretions are not confined to the ductless glands, but are elaborated by the pancreas, kidneys and others. The importance of the external secretions of the pancreas or the pancreatic juice has long been known, but it was only recently (1889) that Mering and Minkowski demonstrated that it furnishes an equally important internal secretion. These observers found that complete extirpation of the pancreas was followed by the appearance of sugar in the urine. This condition obtained even when carbohydrate food was excluded from the diet. Sugar was found to be present when no food was given and persisted during seven days of fasting. With a plentiful supply of food the percentage of sugar may run as high as ten per cent. If only a part of the gland be left or a part even grafted in the abdomen, glycosuria does not occur. This demonstrates then that the glycosuria is not the result of injury in operation nor to the absence of pancreatic secretion from the intestine. These phenomena can only be explained upon the basis of the presence of an internal secretion poured into the blood. After extirpation of the pancreas the last trace of glycogen disappears from the liver. In spite of large quantities of food given, the animals live chiefly at the expense of their own bodies, and in two weeks may lose one-third of their body-weight.

This secretion is thought to be formed by the islands of Langerhans, and is necessary for the normal metabolism of sugar. Opie and Herzog find that in diabetes mellitus in man the islands of Langerhans show signs of hyaline degeneration or may be absent altogether. I find no record of good results from pancreatic injections.

Kidneys.—Certain observed facts indicate that the kidneys not only remove different waste products from the body, but give off to the blood an internal secretion containing one or more substances of vast importance to the body. When they are removed from an animal or rendered functionless in man, within a few days symptoms of a severe uremic poisoning make their appearance. The most natural assumption is that the symptoms are caused by the retention of products otherwise eliminated. But it has been observed that patients have suffered with anuria for days and even weeks without showing any signs of uremia. Bradford removed one kidney from a dog and two-thirds of another at successive operations, which were followed by the death of the dog, although the amount of water and urea eliminated by the remaining portion of the kidney was far above the normal. Brown-Sequard showed that animals from which the kidneys have been removed and which show uremic symptoms are very much benefited by injection of the active extract of the kidney. Moreover, E. Myer has shown that nephrectomized animals, which exhibit periodic respiration resulting from uremia, begin to breath more nearly normally when given a peritoneal injection of kidney extract, or when blood from a normal animal is injected into its veins. These effects have only been temporary, no lasting result having been obtained from the use of kidney extract.

Liver.—Most authors do not seem to consider the liver as having an internal secretion, yet it is an organ without which the animal cannot live, although to be deprived of the bile or external secretion through a fistulous opening does not cause death. As a matter of fact, it does form two products within its cells—glycogen and urea—which are subsequently given off to the blood for purposes of general nutrition or for elimination.

Testes.—It has long been known that castration produces profound and characteristic changes in both men and animals. A steer loses the vehement strength of the bull, and becomes a relatively quiet and tractible animal. If a boy be castrated before puberty his voice does not change as it otherwise would, but remains high-pitched and child-like. The eunuch's muscles do not exhibit the power of endurance of a full-grown man, but are soft and flabby. His body usually has a bloated appearance, and becomes very corpulent. These changes we mention aside from the loss of sexual powers, which indicate that the testes exercise a very marked influence over body metabolism.

A young cock, from which both testes are removed, has testicular substance grafted in the abdominal cavity. The secondary sexual characteristics, otherwise wanting after castration, make their appearance as usual.

On Brown-Sequard's recommendation, extract of testes has found a very extensive use in the treatment of various weakness. It has been shown by experiments that are considered trustworthy, that the extract really favors the action of muscular exercise either by raising the power of the neuro-muscular apparatus, by diminishing its exhaustibility, or by improving its ability to recover. This effect lasts for a long time after the conclusion of the injections and disappears very gradually. Stewart claims that a basic substance, spermin, can be isolated from the extract.

Ovaries.—Certain characteristic changes are said to follow the removal of the ovaries, but not so profound, perhaps, as the castration of the male. It is often stated by gynecologists that castration of a woman is in many cases followed by pronounced corpulency, which indicates that metabolism declines after the operation.

Lowey and Richter confirm this conclusion by a series of experiments on fasting dogs. After the removal of the ovaries the consumption of oxygen fell on the average of 12 per cent., whereas feeding the castrated female's ovarian tissue raised the metabolism in some cases to normal and even above the original level. The ovarian substance produces no effect on the metabolism or normal non-castrated, male or female animals; but on castrated males the increased metabolism is marked, even surpassing that produced by the extract of the testes.

I find that one author who considers the secretion and kinase, substances found in the small intestine, as internal secretions. This is not confirmed, or rather this opinion is not held by all the other physiologists whose works I have consulted.

A RECENT ADDRESS BY REV. W. H. JOHNSTON BEFORE A BODY OF MEDICAL STUDENTS.

Mr. Johnston spoke in part as follows:

Mr. Chancellor, Gentlemen of the Faculty, and the Student Body:

I understand that the young gentlemen before me have come here to prepare themselves for their life work. I am glad to be able to say to you from a personal knowledge, that you have come to the right place. This is not a college *taking* front rank among the medical schools of the land, but it is the one that *has* taken *the* front rank among the medical colleges of *America.*

The privilege of greeting you in such an institution on this auspicious day is peculiarly gratifying to me at this time. I am deeply indebted to your faculty—the really great men that have elevated this institution to its present high and well-deserved position—for this honor they have conferred upon me. I greet you, therefore, and bid you a hearty welcome to this city and to its churches. We are glad to have you among us, and trust we may be mutually beneficial to each other.

When your greatly beloved faculty selected me to deliver this address, they acted wisely—they selected a doctor's friend, aider, and abettor—one of his living, walking advertisements, who has been an unerring index finger pointing many scores of times the afflicted and diseased to the skillful hands and wise heads of the medical fraternity. Yes, when you fell into my hands you fell into the hands of a friend, and I am going to handle you well.

The first question in the catechism is, "Who was the first man?" The answer, of course, is "Adam." And this may be true. My first man, however, was our family physician. Almost the next thing I remember—after my mother's sweet tones had soothed my babyhood into childhood—was the command, "Swallow!" as our doctor caught me by the nape of my neck, and held a spoonful of the bitterest kind of medicine to my tightly-clutched lips. I *swallowed*—and got sound and well. If you don't believe it just look at me. I am a thoroughly-cured man. There was once a poor spindling little preacher on the streets of this city, who was only about six inches in diameter, approached by a countryman with a question, "Mr., can I ax you a question?" "Yes," said the minister, "you can ask as many as you like." "Well, I hope you won't be offended, sir, but I just want to ax you if you ever had the drapsy?" "No," said the minister, "I have never had the dropsy; why do you ask?" "Cause if you ever did, you are the best cured man I ever saw."

But let me whisper it, so low that the uninitiated won't hear, *maybe I would have recovered if I had not swallowed!* But I swallowed then, and I have been swallowing all he has prescribed for forty years. Isn't that wonderful? The confidence we have in these men! If these doctors would but take *my* prescriptions as I take theirs, the dose might be altogether as bitter, and altogether as effectual or more so. Now, today my joy simply knows no bounds, the thing has changed. The worm has turned, the bottom rail is on top, and you folks must do some swallowing. I am delighted.

Medical practice is no new thing. The practice of medicine and some of its results began several thousand years ago. In the Scriptures we read that "Asa," one of the kings of Israel, "was diseased in his feet"—I suppose he had the gout—"and he sought not to the Lord, but to the physicians, and Asa slept with his fathers." This tragedy of Asa is not unique.

I said I was the physician's friend, but I do